American Journal of Medical Genetics 61:42–44 (1996)

# Aplasia Cutis Congenita, High Myopia, and Cone-Rod Dysfunction in Two Sibs: A New Autosomal Recessive Disorder

**Ruth Gershoni-Baruch and Rina Leibo**

*Department of Human Genetics, Rambam Medical Center (R.G.-B.), and the Bruce Rappaport Faculty of Medicine (R.G.-B., R.L.), Haifa, Israel*

**We report on a brother and a sister with congenital nystagmus, cone-rod dysfunction, high myopia, and aplasia cutis congenita on the midline of the scalp vertex. To our knowledge this familial oculocutaneous condition, transmitted as an autosomal recessive trait, has not been reported previously.**


**KEY WORDS: aplasia cutis congenita, autosomal recessive inheritance, high myopia, cone-rod dysfunction**

## INTRODUCTION

Aplasia cutis congenita (ACC) is characterized by a defect in the scalp sometimes extending to the underlying calvaria. In about one-fourth of patients this defect is isolated and not associated with additional clinical manifestations. Most cases are sporadic, although several familial cases have been recorded. The association of ACC with severe ocular defects including myopia, keratoconus, nystagmus, and atrophic pigment epithelium was previously reported in two sibs who also had a peculiar tendency to develop permanent atrophic scars following minor traumas to the skin [Leung et al., 1988].

Here we report on two sibs with congenital nystagmus, cone-rod dysfunction, high myopia, and ACC on the midline of the scalp vertex, an association which to our knowledge was not reported previously.

## CLINICAL REPORTS

Patients 1 and 2 are the only children of a young and consanguineous (2nd cousins) couple of Christian Arab origin. The mother suffered from periodic hypokalemia. Several relatives had children with unrelated fatal MCA syndromes. Yet, on the whole, family history is non-contributory.

### Patient 1

H.C., 3.5-year-old girl, was born at term after an uncomplicated pregnancy and delivery. Birth weight was 3,200 g. The neonatal period was unremarkable. At 40 days of age the parents noticed that the baby failed to fixate. Severe myopia was diagnosed and the infant was provided with spectacles at the age of 3 months. Her physical and psychomotor development seemed adequate. At the age of 3.5 years she was referred for evaluation. Weight was 15 kg (40th centile), height was 96 cm (40th centile), and OFC was 48 cm (25th centile). She had brachycephaly, coarse hair, posteriorly angulated ears, triangular face, flat maxilla, and a small rectangular chin (Fig. 1a). A 1 × 1.5 cm circumscribed midline scalp defect characterised by scarring and alopecia was noted on the vertex (Fig. 1b). The child was somewhat hyperactive and her speech development was slightly delayed. Her psychomotor development was otherwise normal.

Ophthalmological examination disclosed photophobia, horizontal nystagmus, severe myopia (O.D., −14.75; O.S., −15.25), hypopigmented retinae, and an oval depigmented central macular scar surrounded by pigmentary abnormalities. Flash VEP, elicited by bright light stimuli, indicated normal conductance and ERG photopic and scotopic responses were normal.

### Patient 2

H.C., the 1.5-year-old younger brother of patient 1 was born at term following normal pregnancy and delivery. BW was 3,500 g. The neonatal course was uneventful. The infant had severe myopia and congenital nystagmus and was provided with spectacles at the age of 2 months. His physical and psychomotor development seemed adequate.

At the age of 11 months he was referred for evaluation. Weight was 11 kg (50th centile), height was 76 cm (50th centile), and OFC was 45 cm (50th centile). Physical examination disclosed brachycephaly, coarse hair,

Received for publication March 13, 1995; revision received June 12, 1995.

Address reprint requests to Dr. Ruth Gershoni-Baruch, Institute of Human Genetics, Rambam Medical Center, Haifa 35254, Israel.

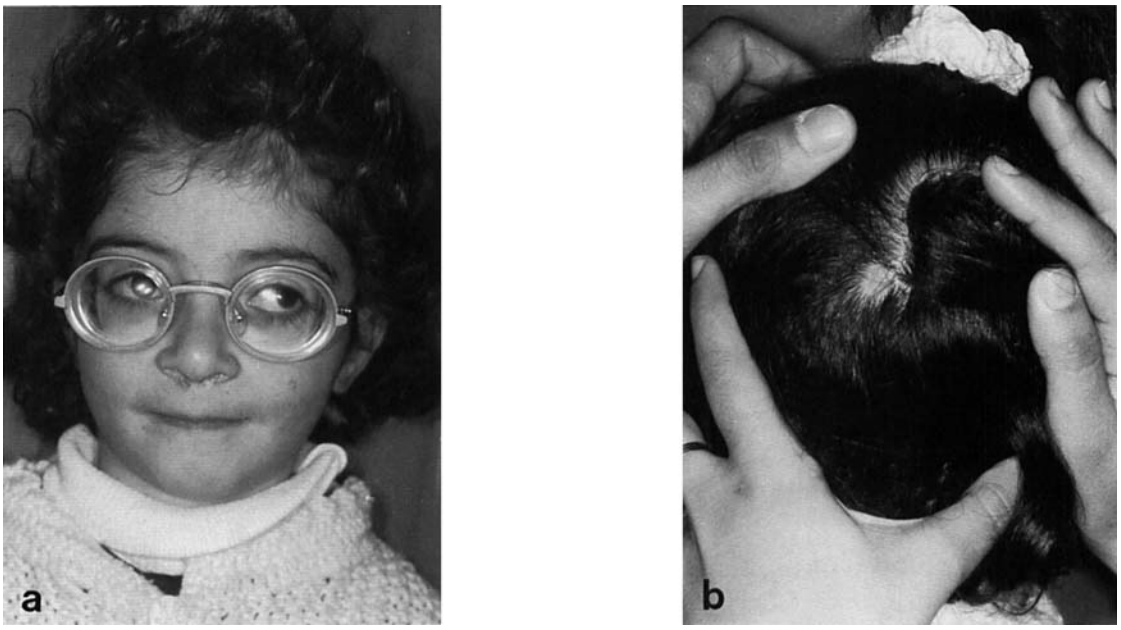


Fig. 1. **a:** Patient 1. **b:** Circumscribed cicatricial alopecia over the vertex.

posteriorly angulated ears, a triangular face, flat maxilla, and a small rectangular chin. A 1 × 1.5 cm circumscribed midline scalp defect characterised by scarring and alopecia was noted on the vertex (Fig. 2b). Ophthalmological examination disclosed photophobia, horizontal nystagmus, severe myopia (OD, −17.25; OS, −18.25), hypopigmented retinae, and and an oval depigmented central macular scar surrounded by pigmentary abnormalities. Flash VEP elicited by bright light stimuli indicated normal conductance; however, ERG photopic and scotopic responses were significantly reduced and abnormally patterned. These findings and the results of the ERG are consistent with the diagnosis of cone-rod dysfunction.

## DISCUSSION

ACC refers to congenital absence of epidermis and, on occasions, hypodermis from one or more areas. The scalp is the commonest site involved, accounting for over 80% of solitary lesions. The lesions are most com-

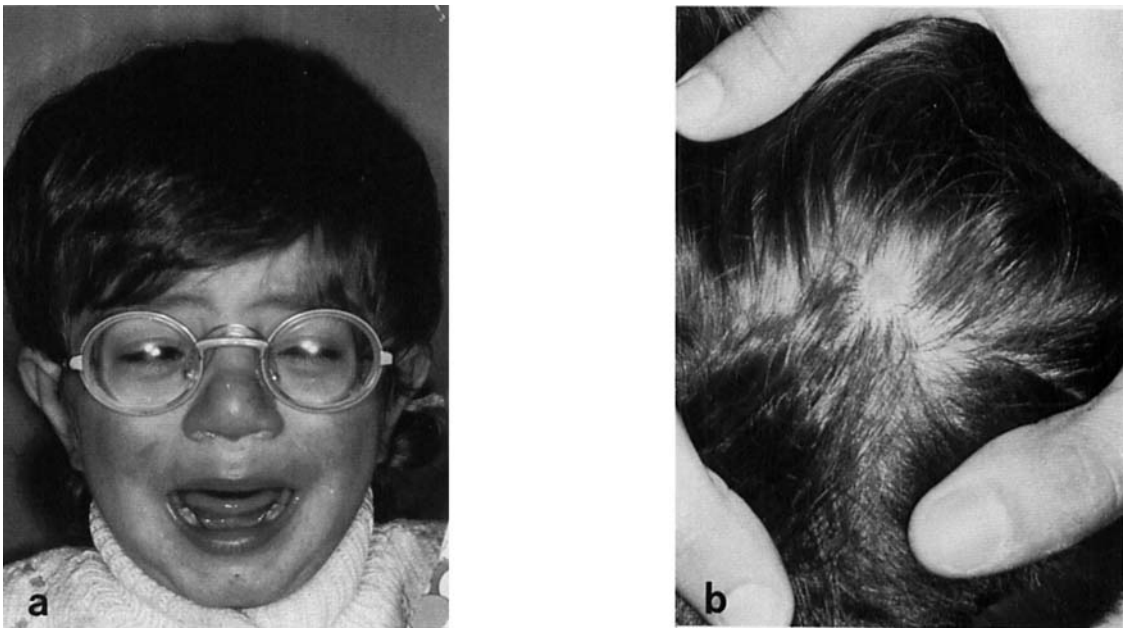


Fig. 2. **a:** Patient 2. **b:** Circumscribed cicatricial alopecia over the vertex.

monly circular, but may be oval, linear, or rhomboidal or even have a stellate configuration. They are commonly present at birth as superficial erosions or deep ulcerations and are sometimes covered by a membranous epithelium filled with serous fluid resembling a blister. Healing with scar formation follows within weeks or months and rarely results in keloidal healing [Frieden, 1986].

ACC is a component manifestation of many syndromes and also occurs on a disruptive, infectious, and teratogenic basis. Association of ACC with many isolated malformations is well documented [Gorlin et al., 1990]. It has also been reported in infants whose mothers took methimazole [Bachrach and Burrow, 1984].

The etiology of the condition is unknown. Tearing off of fetal skin, secondary to amniotic adherence, intrauterine trauma, and infection have apparently been responsible in some cases [Demmel, 1975].

A large number of associated abnormalities have been described with ACC of the scalp, among these are cleft lip and palate, tracheo-oesophageal fistula, congenital heart defects, polycystic kidney, mental retardation, and limb deficiencies [Dallapiccola et al., 1992; Deeken and Caplan, 1970; Gorlin et al., 1990]. Other authors described ocular colobomata and white rings on the cornea in association with the condition [Dugois et al., 1968; Vogel and Kiessling, 1964].

Leung et al. [1988] described two sibs with ACC of the scalp associated with ocular defects such as myopia, keratoconus, nystagmus, atrophic irides, and atrophic pigment epithelium. These children differ from the two sibs described in this report, by their peculiar tendency to develop permanent atrophic linear or macular scars following minor trauma to the forearms, hands and lower legs.

Mantyjarvi et al. [1991] reported on the occurrence of cone-rod dysfunction and high myopia in two brothers and their sister and suggested that they had an hereditary disorder, transmitted by an autosomal recessive trait. In another family this same disorder was reported in six males suggesting X-linked recessive inheritance [Mantyjarvi et al., 1989]. Recently, a gene for cone and rod dysfunction (Aland Island eye disease) was mapped to the proximal short arm of the human X chromosome [Glass et al., 1993].

The association of congenital nystagmus, severe myopia, cone-rod dysfunction, and ACC on the midline of the scalp vertex is unique. Its occurrence in two sibs of both sexes and born to consanguineous parents suggests autosomal recessive inheritance.

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